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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	09/934,020	BRENNER, SYDNEY	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 15, 2007 has been entered.

Status of the Claims

2. Claims 7 and 10 were amended in the amendment to the claims received on July 20, 2006.

Claim 7 was amended in the amendment to the claims received on February 15, 2007.

Claims 1-10 are currently pending.

Claims 7-10 are currently under consideration.

Election/Restrictions

3. Claims 1-6 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 9, 2003.

4. Upon further consideration, the requirement for an election of species in the Restriction requirement mailed on June 26, 2003 is withdrawn.

Priority

5. The present application claims benefit of U.S. provisional application 60/227,058 filed August 21, 2000.

Information Disclosure Statement

6. The copy of the Lisitsyn et al. reference provided on February 15, 2007 was not accompanied by an information disclosure statement. However, the Lisitsyn et al. reference was listed on the IDS and considered by Examiner Tran (previous examiner of record) on March 11, 2003. In order to clarify the record (i.e. the present examiner of record considered the reference), the reference is being listed on the enclosed PTO-892.

Withdrawn Objections

7. The objection to the drawings regarding Fig. 2B (234) is withdrawn in view of applicants amendment to the specification received on February 15, 2007.

Withdrawn Rejections

8. The rejection of claims 7-10 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment to the claims received on February 15, 2007 which provide additional structural and functional information regarding the reagents utilized in the presently claimed method.

9. The rejection of claim 7 under 35 U.S.C. 102(e) as being anticipated by Short et al. U.S. Patent 6,352,842 B1 (filed March 26, 1999) is withdrawn in view of the amendments to the claims received on February 15, 2007.

10. The rejection of claims 7-9 under 35 U.S.C. 102(e) as being anticipated by Barany et al. U.S. patent 6,027,889 (filed May 28, 1997) is withdrawn in view of the amendments to the claims received on February 15, 2007.

11. The rejection of claims 7-10 under 35 U.S.C. 103(a) as being unpatentable over Short et al. U.S. Patent 6,352,842 B1 (filed March 26, 1999) and Strathmann U.S. Patent 6,480,791 B1 (filed October 26, 1999) is withdrawn in view of the amendments to the claims received on February 15, 2007.

12. The rejection of claims 7-10 under 35 U.S.C. 103(a) as being unpatentable over Barany et al. U.S. patent 6,027,889 (filed May 28, 1997) and Barany et al. U.S. Patent 6,534,293 B1 (filed January 5, 2000) is withdrawn in view of the amendments to the claims received on February 15, 2007.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 7-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Method step (b) recites the following: "ligating an Exo III resistant linker to the first cleavage ends of said restriction fragments" wherein the first cleavage ends are produced from restriction endonuclease digestion of genomic nucleic acid. Method step (d) recites the following: "ligating an Exo III susceptible linker…to each said cleavage end" wherein the cleavage end is produced from digesting the first ligation product population with a second restriction endonuclease. Restriction endonuclease digestion of genomic nucleic acid would result in various "first cleavage ends" and "second cleavage end[s]" including populations of nucleic acids with 5' cleavage ends, 3' cleavage ends, and/or both 5' and 3' cleavage ends. Thus it is not clear which ends must have an Exo III resistant or susceptible linker (e.g. 5' ends, 3' ends, or both 5' and 3' ends; some members of the population have linkers on the 5'end only, 3' end only, or on both the 5' and 3' end; both ends of each must have a linker, etc.; please note that conventional designation of the ends have been utilized for dsDNA or partially dsDNA wherein the 5' end is the "left" of the molecule and the 3' end is the "right" of the molecule). Therefore, one of skill in the art would not be able to determine the scope of the presently claimed invention.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 7 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Barany et al. U.S. Patent 6,534,293 filed January 5, 2000 (effective filing date January 6, 1999).

For present claim 7, Barany et al. teach methods of assembling genomic maps of an organism's DNA and identifying polymorphisms comprising (a) digesting genomic DNA from organisms with a restriction endonuclease (i.e. Type II endonuclease wherein the recognition site and cleavage site are coextensive and the restriction fragments have predictable protruding ends) to form restriction fragments with cleavage ends, (b) ligating a linker which is complementary to cleavage ends of step (a) and is Exo III resistant (e.g. 3' overhang), (c) digesting with a second restriction endonuclease (e.g. Type II) which is different from the restriction endonuclease used in step (a) and is specific for methylated cysteine residues (e.g. lower frequency of restriction sites), and (d) ligating a linker with blunt ends which is susceptible to Exo III and comprises a "first member of a binding pair" (e.g. DNA which can hybridize with other DNA); method steps (a)-(d) may occur concurrently in a single tube (e.g. with the understanding by one of skill in the art that method steps (a) and (c) would have to occur at least seconds/minutes prior to method steps (b) and (d); Barany et al. also teach (e) digestion with Exo III to avoid ligation independent PCR amplification (e.g. ssDNA and dsDNA), (f) denaturing and hybridization, and (g) contacting products with "second members of binding pairs" which can be DNA that can hybridize to other DNA (please refer to the entire specification particularly abstract; Figures 5-6, 16-17, 49A, 50A; columns 11-13, 23-29, 80).

For present claim 10, Barany et al. teaches biotin attached to DNA (please refer to entire specification particularly Tables 8-9, 13; column 80).

Therefore, the presently claimed invention is anticipated by the teachings of Barany et al.

17. Claims 7 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Albrecht et al. U.S. Patent 6,013,445 filed October 7, 1997.

The applied reference has a common assignee (i.e. Lynx Therapeutics, Inc.) with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

For present claim 7, Albrecht et al. teach methods of nucleic acid sequence analysis comprising producing libraries of polymorphic sequences via (a) digesting genomic DNA with type II restriction endonucleases (e.g. recognition site and cleavage site coextensive; predictable protruding strands), (b) ligating adaptors with 3' protruding strands and sequences that are complementary to the restriction fragments of step (a) (e.g. 3' protruding strand is Exo III resistant), (c) type II restriction endonuclease digestion (e.g. recognition site and cleavage site coextensive; predictable protruding strands), (d) ligating adaptors with 5' protruding strands and sequences that are complementary to the restriction fragments of step (c) (e.g. 5' protruding strand is Exo III sensitive; the adaptors are "first members of a binding pair"), (e) digestion with T4 polymerase which has 3' to 5' exonuclease activity or "stripping" (e.g. Exo III), (f)

denaturing and hybridization steps, (g) contacting DNA with other DNA to form a hybridization product or alternatively one of the adaptor-tags comprises biotin which can be utilized to purify or capture the nucleic acid fragments (please refer to entire specification particularly abstract; Figures 1A-1E, 2, 3A-3B; columns 2, 5-24, 26-27, 30, 32; Examples 1-2).

For present claim 10, Albrecht et al. teach biotin attached to the tag/adaptor complex (please refer to entire specification particularly columns 8, 26, 30; Figure 2).

Therefore, the presently claimed invention is anticipated by the teachings of Albrecht et al.

18. Claims 7-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Stanton, Jr. U.S. Patent 6,475,736 effective filing date May 23, 2000.

For present claim 7, Stanton, Jr. teaches methods for determining genotypes and haplotypes requiring production of reference libraries comprising (a) digestion with Type II restriction enzymes (e.g. recognition site and cleavage site are coextensive; predictable protruding ends), (b) protecting the fragments from exonuclease digestion via either ligating adaptors which protect the fragments from exonuclease activity or via selecting restriction enzymes which produce ends that are not susceptible to exonuclease digestion (e.g. Exo III resistant; 3' protruding strand and a strand complementary to the fragment of step (a)), (c) digestion with Type II restriction enzymes (e.g. recognition site and cleavage site are coextensive; predictable protruding ends), (d) producing exonuclease susceptible ends via either ligating adaptors which are susceptible to exonuclease activity or selecting a restriction enzyme that will produce ends that are susceptible to exonuclease (e.g. Exo III susceptible; 5' protruding

strand or blunt end and a strand complementary to the fragment of step (c); DNA of adaptor is a first member of a binding pair), (e) Exonuclease III digestion, (f) denaturation and hybridization via PCR; (g) capture of fragments via biotin-streptavidin beads (please refer to entire specification particularly Figures 18-20; columns 5-14, 20, 25, 28, 34-35, 39, 43-50, 53-56; Examples 1-3).

For present claims 8-9, Stanton, Jr. teaches utilizing both exonuclease I and exonuclease III (please refer to entire specification particularly column 54).

For present claim 10, Stanton, Jr. teaches biotin attached to DNA in order to capture the DNA fragments (please refer to entire specification particularly column 39, 47-50).

Therefore, the presently claimed invention is anticipated by the teachings of Stanton, Jr.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. U.S. Patent 6,534,293 filed January 5, 2000 (effective filing date January 6, 1999) and Barany et al. U.S. Patent 7,166,434 (effective filing date May 28, 1997).

For present claim 7, Barany et al. (6,534,293) teach methods of assembling genomic maps of an organism's DNA and identifying polymorphisms comprising (a) digesting genomic DNA from organisms with a restriction endonuclease (i.e. Type II endonuclease wherein the

recognition site and cleavage site are coextensive and the restriction fragments have predictable protruding ends) to form restriction fragments with cleavage ends, (b) ligating a linker which is complementary to cleavage ends of step (a) and is Exo III resistant (e.g. 3' overhang), (c) digesting with a second restriction endonuclease (e.g. Type II) which is different from the restriction endonuclease used in step (a) and is specific for methylated cysteine residues (e.g. lower frequency of restriction sites), and (d) ligating a linker with blunt ends which is susceptible to Exo III and comprises a "first member of a binding pair" (e.g. DNA which can hybridize with other DNA); method steps (a)-(d) may occur concurrently in a single tube (e.g. with the understanding by one of skill in the art that method steps (a) and (c) would have to occur a least seconds prior to method steps (b) and (d); Barany et al. also teach (e) digestion with Exo III to avoid ligation independent PCR amplification (e.g. ssDNA and dsDNA), (f) denaturing and hybridization, and (g) contacting products with "second members of binding pairs" which can be DNA that can hybridize to other DNA (please refer to the entire specification particularly abstract; Figures 5-6, 16-17, 49A, 50A; columns 11-13, 23-29, 80).

For present claim 10, Barany et al. (6,534,293) teaches biotin attached to DNA (please refer to entire specification particularly Tables 8-9, 13; column 80).

However, Barany et al. (6,534,293) does not teach utilizing both Exo III and Exo I.

For present claims 8-9, Barany et al. (7,166,434) teach that both Exo III and Exo I can be utilized in methods for the production and identification of polymorphisms.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the methods of assembling genomic maps of an organism's DNA

and identifying polymorphisms taught by Barany et al. (6,534,293) with Exo I taught by Barany et al. (7,166,434).

One having ordinary skill in the art would have been motivated to do this because Barany et al. (7,166,434) teach that a combination of Exo III and Exo I would be useful because Exo III is specific for double stranded DNA while Exo I is specific for single stranded DNA therefore in the LDR/PCR reactions utilized by Barany et al. Exo I and Exo III would digest both the target and probe while leaving the ligation product undigested (please refer to column 26, lines 18-56).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the methods of assembling genomic maps of an organism's DNA and identifying polymorphisms taught by Barany et al. (6,534,293) with Exo I taught by Barany et al. (7,166,434) because of the various examples taught by Barany et al. (6,534,293) utilizing the adaptors and restriction enzyme digestion (please refer to Figures 5-6, 16-17, 49A, 50A; Examples 1-6) and the methods taught by Barany et al. (7,166,434) utilizing Exo I (please refer to Figures 13-17; claim 11).

Therefore, the modification of the methods of assembling genomic maps of an organism's DNA and identifying polymorphisms taught by Barany et al. (6,534,293) with Exo I taught by Barany et al. (7,166,434) render the instant claims *prima facie* obvious.

Conclusion

21. The art made of record and not relied upon is considered pertinent to applicant's disclosure (U.S. Patent 6,897,023).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ADS
April 23, 2007

MARK L. SHIBUYA
PRIMARY EXAMINER